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NO PYROSYNTHESIS OF NNN AND NNK FROM NICOTINE

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N'-Nitrosornornicotine (NNN) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) are powerful and organspecific carcinogens, which have been found in tobacco and tobacco smoke in relatively high concentrations. NNN is either formed by nitrosation of the major tobacco alkaloid nicotine under loss of a methylgroup or by nitrosation of the minor alkaloid nornicotine. NNK can only derive from nicotine by oxidative N-nitrosation. In order to reduce smokers burden with NNN and NNK it is essential to know origin and pathways of their formation. During curing and fermentation of tobacco, the tobacco alkaloids can react with nitrite, which is formed by microbial reduction of nitrate, to yield tobacco-specific nitrosamines (TSNA). Nitrate also gives rise to nitrogen oxides in smoke which are supposed to react with the tobacco alkaloids during smoking. Thus the presence of NNN and NNK in mainstream smoke was explained qby their direct transfer from tobacco into the mainstream smoke and by their formation during smoking (pyrosynthesis). The purpose of this investigation was to investigate the contribution of a possible pyrosynthesis to the TSNA burden os smokers.

Spiking of cigarettes with the TSNA precursors nitrate and nicotine prior to smoking (nitrate spiking level: 4-20 mg/cigarette, nicotine spiking level: 10 mg/cigarette) did not result in a measurable increase of NNN and NNK in mainstream smoke. After spiking cigarettes with radioactive labelled nicotine neither radioactive labelled NNN nor radioactive labelled NNK could be detected in the mainstream smoke. Furthermore the concentrations of NNN and NNK in mainstream smoke and in tobacco were determined for commercial cigarettes and the ratios between the mainstream smoke concentration and the level of preformed NNN and NNK were calculated for West German nonfilter cigarettes. These ratios were constant and did neither depend on the nicotine nor on the nitrate level of the tobacco except for NNK in dark tobacco type cigarettes.

The nitrosation potential of freshly generated mainstream smoke was investigated by addition of nornicotine and nicotine to the trapping fluids for the mainstream smoke. Nitrosation of the secondary amine nornicotine could be observed, whereas nicotine nitrosation could not be detected under these conditions. Furthermore model studies on the exposure of nicotine to nitrogen oxides have been carried out. At a total nitrogen oxide concentration of 400 ppm with varying composition of nitric oxide and nitrogen dioxide (400 ppm NO/no NO₂ - 240 ppm NO/160 ppm NO₂) only small amounts of NNN and NNK were formed.

These data indicate that nicotine cannot easily be nitrosated during smoking to form NNN and NNK. Pyrosynthesis of NNN and NNK from nicotine does not occur for standard cigarette types. The NNN and NNK burden of smokers is given by the amount of preformed NNN and NNK in tobacco.